Targeted Research Area: Endocrine Disrupters

General Information on Endocrine Disrupters

- **Prevalence and incidence of Endocrine Disrupters:**
  - Surveillance studies show an increasing incidence in potentially hormone-related conditions (hypospadias, cryptorchicism, testicular cancer, prostate cancer) in Canada and the U.S.[35]
  - In 1996, the U.S. EPA identified endocrine disruption as an environmental health problem. The incidence of testicular cancer has increased in almost all countries with reliable cancer registries.[36]
  - The incidence of endometriosis has been increasing over the past 25 years in developing countries. Hypospadia is one of the most common congenital anomalies. Data from five European countries and two U.S. surveillance systems reported unexplained increases in the rate of hypospadias from 1968 to 1993.[37]
- **Mortality from Endocrine Disrupters:** This information was not readily available to Lewin.
- **Disease severity/disease burden:** Endometriosis accounts for one-half million hospital bed-days in the U.S. (1980).[38]
- **Cost to individual/family/society/healthcare system** : This information was not readily available to Lewin.
- **Frequency/load of exposure:** This information was not readily available to Lewin.
  - Humans are exposed to endocrine disrupters through various routes (food, air, water, soil, pesticides, etc.). Neonatal exposures to phytochemicals occurs through bovine milk, and soy-based milk substitutes contain even greater amounts. The plasma concentration of genistein in infants soy-based formulas was, on average, 200 times greater than measured in infant-fed cow's milk formula and 300 times greater than in human breast milk.[39]
- **Special Populations:** Although many have been banned in the U.S., chemicals that have been identified as having endocrine-like activity still exist in many countries, and most persist for a long time in the environment. The south Atlantic region of the U.S. has the highest overall environmental levels of 54 toxic substances, including PCBs and dioxins.[40]

Hypothesis #11, described on the following pages, is associated with the Endocrine Disrupters targeted research area.

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[35] Solomon GM, Schettler T. Environment and health: 6. Endocrine disruption and potential human health implications. Canadian Medical Association Journal 2000 Nov 28;163(11):1471-6.

[36] Weber RFA, Pierik FH, Dohle GR, Burdorf A. Environmental influences on male reproduction. BJU International 2002;89(2):143-148.

[37] Rubin CH, Niskar AS. Endocrine disruptors: an emerging environmental health problem. Journal of the Medical Association of Georgia 1999 Dec;88(4):27-30.

[38] Ibid.

[39] Akingbemi BT, Hardy MP. Oestrogenic and antiandrogenic chemicals in the environment: effects on male reproductive health. Annals of Medicine 2001;33(6):391-403.

[40] Rubin CH, Niskar AS. Endocrine disruptors: an emerging environmental health problem. Journal of the Medical Association of Georgia 1999 Dec;88(4):27-30.

Hypothesis #11: Increased fetal exposure to endocrine disrupters may result in reproductive and physiological abnormalities.

General Information Related to Hypothesis #11

- **Findings from the recent research (targeted search):** Information reported in the following four studies contributed to the above-mentioned hypothesis.

Study #1: Eskenazi B, Bradman A, Castoria R. Exposures of children to organophosphate pesticides and their potential adverse health effects. Environmental Health Perspectives 1999;107(3):409-419.

Study #1 hypothesis being tested: A higher incidence of urogenital abnormalities among male newborns and decline in qualitatively normal sperm may be due to a disruption of reproductive development caused by endocrine disrupters.

Study #1 findings: There is evidence that humans have been exposed to endocrine disrupters present in the environment. Significant levels of endocrine disrupters have been detected in human tissues and have been associated with developmental and reproductive anomalies in laboratory species. Urogenital anomalies in newborns, testicular cancer, and impaired sperm viability may be a result of the effect of exogenous endocrine disrupters. In addition to an oral route, investigation of the effects of dermal and inhalation exposure are also required. However, no direct evidence currently shows that endocrine disrupters in the environment affect humans.

Study #2: Rubin CH, Niskar AS. Endocrine disrupters: an emerging environmental health problem. Journal of the Medical Association of Georgia 1999;88(4):27-30.

Study #2 hypothesis being tested: Accumulation of an endocrine disrupter in the environment can cause adverse health effects, including birth defects, cancer, impaired fertility, and developmental disabilities.

Study #2 findings: Although clinical use of exogenous estrogens has been associated with impaired fertility, e.g., endometriosis, studies have not conclusively shown an association in humans. Hormone-like chemicals (PCBs and dioxins) in the environment may be responsible for some of the increased incidence of endometriosis. Hypospadias, the abnormal placement of the urethral opening on the penile shaft, is influenced by in utero hormonal levels and may be associated with human exposure to environmental chemicals that interfere with normal testosterone activity.

Study #3: Solomon GM, Schettler T. Environment and health: 6. Endocrine disruption and potential human health implications. Canadian Medical Association Journal 2000;163(11):1471-6.

Study #3 hypothesis being tested: There is an association between occupational exposure to solvents or pesticides and adverse effects on offspring such as hypospadias or cryptorchidism.

Study #3 findings: Studies in humans and laboratory animals have found associations between exposure to specific pesticides or chemicals and levels of thyroid stimulating hormone and abnormal sexual behavior or feminization of males. However, population-based epidemiologic studies relevant to endocrine disruption are still few and limited by the time lag between exposure and clinical disease, difficulty of defining exposure and control populations, poor retrospective assessment of exposures during the prenatal period. Also a clearer understanding of gene-environment interactions is needed. Opinions of researchers vary whether endocrine disrupters at current exposure levels affect human health or if suggestive evidence is enough to call for increased action to shield from endocrine disrupters.

Study #4: Weber RFA, Pierik FH, Dohle GR, Burdorf A. Environmental influences on male reproduction. BJU International 2002;89(2):143-148.

Study #4 hypothesis being tested: The increasing incidence of reproductive abnormalities (poor semen quality, hypospadias, testicular cancer) in males may be related to increased estrogen exposure in utero. Increased exposure to endocrine disrupters during fetal life may disrupt development of testis and the rest of the male reproductive tract.

Study #4 findings: Findings are inconclusive due to insufficient human studies with controlled comparisons, especially with all-male populations. With regard to declining sperm quality, most study populations reviewed cannot be regarded as representative of the normal population. Furthermore, other complicating factors (illnesses, variation in scrotal temperature due to clothing) are not addressed in studies. Sufficient evidence exists that reproductive disruption in wildlife may be caused by environmental pollutants, specifically by endocrine-disrupting compounds; however, only circumstantial evidence exists for most compounds.